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Radical chemotherapy of massively disseminated testicular cancer in a 24-year-old patient with acute renal failure and cancer cachexia — case report

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ABSTRACT

We present a case of a 24-year-old patient with metastatic testicular cancer, with massive dissemination to the lung, mediastinum, and abdominal organs, generalised lymphadenopathy, and accompanying acute renal failure due to the compression of the ureters by lymph node conglomerates. The patient underwent radical chemotherapy — initially at doses adequate for renal function together with periodically applied haemodialysis, subsequently in full doses. Two lines of the chemotherapy were applied. The cycles were administered according to the planned rhythm with no deferrals. The applied treatment resulted in relief of the symptoms of the disease and partial regression of the lesions in imaging studies. The persistent lesions have presented no signs of progression since November 2016 to the present day.

Key words: testicular cancer, radical chemotherapy, acute renal failure

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Case study

A 24-year-old patient with cancer of the only remaining right testicle after orchidectomy performed in March 2016 (germ cell tumour — mixed embryonal carcinoma and teratoma) was referred to the Department of Clinical Oncology in May 2016 for systemic treatment. Medical history: condition following removal of the left testicle due to torsion ten years ago. In the imaging study from March 2016 massive dissemination to the lungs, mediastinal lymph nodes, liver, and extraperitoneal lymph nodes in the abdominal cavity and pelvis, with compression and occlusion of the inferior cava vein, and compression of both ureters were described.

On admission the patient was in a severe general condition (ECOG 4), with tumour cachexia, generalised lymphadenopathy, massive oedema, and acute extrarenal failure of the kidneys (creatinine 1259 $\mu\text{mol/L}$). On the first day of hospitalisation haemodialysis was started.

The clinical picture indicated that the renal failure was the result of ureteral congestion by lymph node conglomerates, and the implementation of chemotherapy would result in improved renal function; therefore, nephrostomy was abandoned, given that it would have been a potential source of infection. Due to the general condition of the patient, the disseminated tumour process and obstruction of the inferior cava vein, low molecular weight heparin was used at preventive doses since the beginning of treatment. Due to the patient's cachexia and eligibility for urgent chemotherapy, parenteral nutrition (SmofKabiven 1100 kcal/day, Vitalipid N, Soluvit N, Addamel N, KCl 60 mEq) had been used since the first day of stay.

On Day 4 of the stay, chemotherapy from the life-saving indications was initiated according to the BEP regimen in doses adequate to the renal function (GFR 4 mL/min/1.7 m²), with primary prophylaxis of neutropenic fever. On the seventh day of hospitalisation the

urinary retention retreated, and the patient entered the polyuria phase of renal failure. On the 13th day of the patient's stay neutropenic fever occurred, so empiric antibiotic therapy was applied (vancomycin, meropenem). During the first 38 days of hospitalisation the patient was administered two cycles of BEP chemotherapy, a total of six units of red cell concentrate and one unit of thrombocyte concentrate were transfused, and parenteral nutrition was administered for 22 days. The patient was discharged in good condition (ECOG 0).

BEP chemotherapy was continued for four cycles; all components of the BEP regimen from the beginning of therapy were administered according to rhythm, without deferral and dose reduction. The patient required transfusions of blood components several times.

In September 2016, awaiting surgical consultation for retroperitoneal lymphadenectomy, due to clinical progression in the development of lymphedema of the lower limbs, despite PR in imaging studies, chemotherapy was started with the TIP regimen, which continued until November 2016 (four cycles) with partial response according to RECIST 1.1 in imaging studies. Then, due to survival lesions, the patient was referred to the Urology Clinic of the Institute of Oncology in Warsaw to qualify for retroperitoneal lymphadenectomy. The patient was not qualified for surgical treatment — the lesions were assessed as non-operative. It was decided to continue the patient's observation.

Until now, the patient remains in an ECOG 0 general condition without progressive features.

Discussion

Testicle cancer accounts for 1–3% of malignant neoplasms in men in western countries; however, among young males aged 15–34 years it is the most common malignant neoplasm in many European countries [1]. Germ cell tumours are associated with a good prognosis — cure rates range from almost 100% in patients with stage I to approx. 80% in cases of generalised disease [2]. In the group of patients with non-seminoma neoplasms with an unfavourable prognosis according to IGCCCG, as in the case of this patient, the survival rate of five years is 50% [3].

Chemotherapy of testicular cancer, regardless of its severity, should be carried out with the intention of curing. In the case of this patient, the treatment was applied at the required doses and without deferral. In the course of the patient's therapy anaemia and thrombocytopenia were observed, and blood components were transfused several times to maintain the planned rhythm of the treatment.

In the third stage of clinical progression, standard treatment includes the application of a three-cycle BEP

regimen in patients with favourable IGCCCG prognosis or four cycles in an intermediate prognosis. There are only single reports on the management of testicular cancer chemotherapy in patients with impaired renal function [4]. In the case under discussion, in the first BEP cycle, cisplatin was replaced by carboplatin at a dose calculated using Calvert's formula, which takes into account the renal function expressed by creatinine clearance. After normalisation of creatinine concentration levels, as of the second cycle, treatment was applied according to the standard cisplatin-based BEP regimen. In the fourth TIP cycle an increase in creatinine concentration (253 $\mu\text{mol/L}$, GFR 28 mL/min/1.7 m²) was observed again; therefore, on the first day of the cycle paclitaxel was administered in the required doses, and then after a week of fluid therapy, when improvement was achieved in GFR (62 mL/min/1.7 m²), it was decided that ifosfamide-based chemotherapy would be applied and administration of a platinum derivative was abandoned. In the literature, there is also a description of a case of a patient suffering from testicle cancer with accompanying renal and hepatic dysfunction, who had been treated with nedaplatin, a second-generation platinum derivative, in place of cisplatin in the BEP regimen [4], which is characterised by lower nephrotoxicity.

Bleomycin is metabolised in the kidneys in 60% [5]; therefore, according to some authors in the case of patients with reduced glomerular filtration, dose reduction should be considered, depending on the creatinine clearance value [5]. Etoposide, in turn, is eliminated by both the liver and the kidney. Due to the possibility of compensatory elimination of the etoposide in patients with hepatic and/or renal dysfunction, doses of etoposide in these patients have not been clearly defined. Where creatinine concentration is greater than 1.4 mg/dL, a 30% reduction in the etoposide dose should be considered [5].

In the case of this patient, clinical progression was observed in a period of less than three months after treatment with a platinum derivative. However, according to the authors, taking into account the massive character of neoplastic lesions observed before the beginning of treatment, the good response to BEP chemotherapy, and rapid regression of the lesions, it is possible to talk about the sensitivity to treatment with platinum derivatives. Therefore, it was decided to implement TIP chemotherapy in the second treatment line — as in the case of patients sensitive to platinum.

In the case of progression of non-seminoma neoplasms of the testicle, retroperitoneal lymphadenectomy should also be considered due to the possible presence of lesions in other locations. The application of cisplatin-based chemotherapy, followed by surgical resection to remove residual lesions, makes it possible to obtain total survival rates ranging from 80% to 90% [6]. The resection of lesions after chemotherapy was

considered in the patient's case; however, due to the lack of a possibility of a radical resection of the lesions, surgical treatment was abandoned.

In conclusion, the radical therapeutic approach and the use of adjunctive therapy facilitated not only improvement of the clinical condition of the patient, who initially had been at the limits of organ efficiency, but also obtaining of a significant regression of massive metastatic changes. Survival changes persist without progression as of November 2016 to the present day.

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